K121710

510(k) Summary

DEC 2 7 2012

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid® 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 400-8460 Fax number: (408) 541-6439
Contact:	Kerry J. Flom, Ph.D.
Date of Preparation:	December 26, 2012
Device:	
Trade name:	Xpert® CT/NG
Common name:	Xpert CT/NG Assay
Type of Test:	Automated, multiplex real-time polymerase chain reaction (PCR) assay intended for the *in vitro* qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG).
Regulation number/ Classification name:	866.3120/ Chlamydia serological reagents. 866.3390/ Neisseria spp. direct serological test reagents
Product code:	MKZ LSL
Classification Advisory Panel	Microbiology (83)
Predicate Devices - Assay:	GEN-PROBE® APTIMA® Combo 2 Assay [510(k) #K043224] Becton Dickenson ProbeTec™ ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay [510(k) #K012351]
Predicate Devices – Ancillary Specimen Collection Kits:	GEN-PROBE® APTIMA® Combo 2 Assay [510(k) #K043244] for use with: GEN-PROBE® APTIMA® Unisex Swab Specimen Collection Kit for Endocervical and Urethral Swab Specimens GEN-PROBE® APTIMA® Urine Specimen Collection Kit for Male and Female Urine GEN-PROBE® APTIMA® Vaginal Swab Specimen Collection Kit for Male and Female Urine

Device Description:

The Xpert CT/NG Assay is an automated *in vitro* diagnostic test for qualitative detection and differentiation of DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG). The assay is performed on the Cepheid GeneXpert Instrument Systems. The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequences in simple or complex samples using real-time PCR and RT-PCR assays. The systems consist of an instrument, personal computer, and preloaded software for running the tests on collected samples and viewing the results. The system requires the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between cartridges during the testing process is minimized.

The Xpert CT/NG Assay includes reagents for the 5' exonuclease real-time PCR detection and differentiation of CT and NG. Reagents for the detection of a Sample Processing Control (SPC), a Sample Adequacy Control (SAC), and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the target bacteria and to monitor the presence of inhibitors in the PCR reaction. The SAC reagents detect the presence of a single copy human gene and monitor whether the specimen contains human DNA. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability. The primers and probes in the Xpert CT/NG Assay detect chromosomal sequences in the bacteria. One target is detected for CT (CT1) and two different targets are detected for NG (NG2 and NG4). Both NG targets need to be positive for the Xpert CT/NG Assay to return a positive NG result.

The GeneXpert Instrument Systems, comprised of the GeneXpert Dx Systems, the GeneXpert Infinity-48 System and the GeneXpert Infinity-80 System, have 1 to 80 randomly accessible modules, depending upon the instrument, that are each capable of performing separate sample preparation and real-time PCR tests. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time PCR and detection.

The ancillary specimen collection kits for use with the Xpert CT/NG Assay are the Cepheid® Xpert® CT/NG Vaginal/Endocervical Specimen Collection Kit and the Cepheid® Xpert® CT/NG Urine Specimen Collection Kit.

Device Intended Use:

Xpert CT/NG Assay:

The Xpert® CT/NG Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) to

aid in the diagnosis of chlamydial and gonorrheal urogenital disease. The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, endocervical swab, and patient-collected vaginal swab (collected in a clinical setting).

Ancillary Collection Kits:
The Cepheid® Xpert® CT/NG Vaginal/Endocervical Specimen Collection Kit is designed to collect, preserve and transport patient *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in endocervical and vaginal specimens from symptomatic and asymptomatic individuals prior to analysis with the Cepheid Xpert CT/NG Assay.

The Cepheid Xpert CT/NG Vaginal/Endocervical Specimen Collection Kit has only been cleared for use with the Cepheid Xpert® CT/NG Assay.

The Cepheid® Xpert® CT/NG Urine Specimen Collection Kit is designed to preserve and transport *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in first-catch male and female urine specimens from symptomatic and asymptomatic individuals prior to analysis with the Cepheid Xpert CT/NG Assay.

Substantial Equivalence:
The Xpert CT/NG Assay is substantially equivalent to the following predicate assays:

- K043224: GEN-PROBE® APTIMA® Combo 2 Assay, Gen-Probe Inc.
- K012351: Becton Dickenson ProbeTec™ ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay, Becton Dickenson & Co.

Similarities and differences between the Cepheid Xpert CT/NG Assay and the predicate devices are shown in Table 1.

A clinical study at thirty-six collection sites was conducted to compare Xpert CT/NG Assay performance relative to a patient infection status algorithm, based on results from the GEN-PROBE APTIMA Combo 2 Assay and Becton Dickenson ProbeTec ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay tests.

Table 1: Comparison of Similarities and Differences of the Xpert CT/NG Assay with the Predicate Devices

	Device	Predicates	
Item	**Cepheid Xpert CT/NG Assay**	**GEN-PROBE® APTIMA® Combo 2 Assay**	**Becton Dickenson ProbeTec™ ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay**
510(k) No.	To be assigned	K043224	K012351
Regulation	866.3120, 866.3390	866.3120, 866.3390	866.3120, 866.3390
Product Code	MKZ, LSL	MKZ, LSL	MKZ, LSL
Device Class	I, II	I, II	I, II
Technology/ Detection	Multiplex real-time polymerase chain reaction (PCR)	Multiplex transcription-mediated amplification (TMA)	Multiplex strand displacement amplification (SDA)
Intended Use	An automated, multiplex real-time RT-PCR assay, performed on the GeneXpert Instrument Systems, intended for the *in vitro* qualitative and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) to aid in the diagnosis of chlamydial gonorrheal urogenital disease. The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, endocervical swab, and patient-collected vaginal swab (collected in a clinical setting).	A target amplification nucleic acid probe test that utilizes target capture for the *in vitro* qualitative detection and differentiation of ribosomal RNA (rRNA) from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) in clinician-collected endocervical, vaginal, and male urethral swab specimens, patient-collected vaginal swab specimens*, and female and male urine specimens. The assay is also intended for use with testing of gynecological specimens collected in the PreservCyt Solution and processed with the Cytyc ThinPrep 2000 System. The assay may be used to test specimens from	Strand Displacement Amplification (SDA) technology for the direct, qualitative detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in endocervical swabs, male urethral swabs, and in female and male urine specimens as evidence of infection with C. *trachomatis, N. gonorrhoeae,* or of co-infection with both C. *trachomatis* and *N. gonorrhoeae.* Specimens may be from symptomatic or asymptomatic females and males. A separate Amplification Control is an option for inhibition testing (BDProbeTec™ ET *CT/GC/AC* Reagent Pack).

	Device	Predicates	
Item	**Cepheid Xpert CT/NG Assay**	**GEN-PROBE® APTIMA® Combo 2 Assay**	**Becton Dickenson ProbeTec™ ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay**
		symptomatic and asymptomatic individuals to aid in the diagnosis of gonococcal and/or chlamydial urogenital disease. *Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The vaginal swab specimen collection kit is not for home use.	
Indication for Use	Asymptomatic and symptomatic patients	Same	Same
Assay Targets	DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG)	ribosomal RNA (rRNA) from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC)	DNA from *Chlamydia trachomatis* (CT) and *Neisseria gonorrhea* (NG)
Specimen Types	Urine, endocervical swab, and patient-collected vaginal swab	Clinician-collected endocervical, vaginal, and male urethral swab specimens, patient-collected vaginal swab specimens, and female and male urine specimens	Endocervical swabs, male urethral swabs, and urine specimens for females and males
CT Analyte Targets	CT genomic DNA	CT ribosomal RNA	CT cryptic plasmid DNA
NG Analyte Targets	NG genomic DNA	NG ribosomal RNA	NG genomic DNA

	Device	Predicates	
Item	**Cepheid Xpert CT/NG Assay**	**GEN-PROBE® APTIMA® Combo 2 Assay**	**Becton Dickenson ProbeTec™ ET *Chlamydia trachomatis /Neisseria gonorrhoeae* Amplified DNA Assay**
Collection Kit	Urine collection kit Swab collection kit	Urine collection kit Swab collection kit	Urine collection kit Swab collection kit
Technological Principles	RT/PCR	TMA	SDA
Nucleic Acid Extraction	Yes	Yes	Yes
Sample Extraction	Self-contained and automated after specimen sample elution and two single-dose reagent additions.	Manual	Manual
Assay Results	Qualitative	Qualitative	Qualitative
Instrument System	Cepheid GeneXpert Instrument Systems	Gen-Probe Leader HC+ luminometer and Gen-Probe Target Capture System	ProbeTec™ ET System
Assay Controls	Internal sample processing control (SPC), sample adequacy control (SAC), and probe check control (PCC). External controls available.	The Positive Control, CT / Negative Control, GC and the Positive Control, GC / Negative Control, CT act as controls for the target capture, amplification, and detection steps of the assay.	Amplification Control (AC)
Rapid test results	Approximately 90 minutes (1.5 hours) to results.	Approximately 4.5 hours to results.	Approximately 3.5 hours to results.

The Ancillary Specimen Collection Kits are substantially equivalent to the following predicate assays:

- GEN-PROBE® APTIMA® Unisex Swab Specimen Collection Kit for Endocervical and Urethral Swab Specimens [in 510(k) #K043144]
- GEN-PROBE® APTIMA® Urine Specimen Collection Kit for Male and Female Urine [in 510(k) #K043144]

- GEN-PROBE® APTIMA® Vaginal Swab Specimen Collection Kit for Male and Female Urine [in 510(k) #K043144]

Similarities and differences between the Cepheid Collection Kits and the predicate Collection devices are shown in Table 2.

Table 2: Comparison of Similarities and Differences of the Xpert CT/NG Collection Kits with the Predicate Device Collection Kits

	Device :	**Predicate:**	**Predicate:**
Item	**Cepheid Xpert CT/NG Vaginal/Endocervical Specimen Collection Kit**	**GEN-PROBE® APTIMA® Unisex Swab Specimen Collection kit for Endocervical and Male Urethral Swab Specimen**	**GEN-PROBE® APTIMA® Vaginal Swab Specimen Collection kit**
Description	Contains an individually packaged sterile large cleaning swab (for endocervical samples) and a package containing an individually packaged sterile collection swab (for vaginal and endocervical sampling) and a Xpert CT/NG Swab Transport Reagent tube. The collection swab is placed into the Transport Reagent Tube after swab sampling to stabilize the nucleic acid until sample preparation.	Contains an individually packaged sterile Endocervical cleaning swab and an individually-packaged sterile specimen collection swab that is placed into the Transport Tube after swab sampling and is used to stabilize the nucleic acid until sample preparation.	Contains an individually packaged sterile specimen collection swab that is placed into the Transport Tube after swab sampling and is used to stabilize the nucleic acid until sample preparation.

Item	**Cepheid Xpert CT/NG Urine Specimen Collection Kit**	**GEN-PROBE® APTIMA® Urine Specimen Collection kit**
Description	Contains one individually packaged sterile disposable transfer pipette and one Xpert CT/NG Urine Transport Reagent tube. Approximately 7 mL of a first-catch urine specimen is transferred to the Urine Transport Reagent tube to preserve and transport the specimen prior to analysis with the Cepheid Xpert CT/NG Assay.	Contains a disposable transfer pipette for adding approximately 2 mL of urine to a Specimen Transport Tube containing 2.0 mL of Transport Buffer.

Non-Clinical Studies:

Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert CT/NG Assay with purified CT elementary bodies seeded into negative natural human pooled vaginal swab and pooled male urine matrices, and NG cells seeded into negative pooled simulated swab and pooled male urine matrices.

Pooled Vaginal Swab Matrix

Elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were purified by centrifugation through a 30% sucrose cushion and titered by enumeration of elementary bodies by transmission electron microscopy. Each serovar was diluted into pooled negative vaginal swab matrix and tested with the Xpert CT/NG Assay. Replicates of 20 were evaluated at eight concentrations for CT serovar D and at seven concentrations for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies in vaginal swab matrix is 84 EB/mL. The claimed LoD for purified CT serovar H elementary bodies in vaginal swab matrix is 161 EB/mL (Table 3). In this study, LoDs for the remaining purified CT serovars (in EB/mL) are A (600), B (6), Ba (1900), C (34), E (6), F (202), G (96), I (21), J (150), K (117), LGV I (31), LGV II (20) and LGV III (210) EB/mL.

Table 3: LoD of Two CT Serovars in Pooled Vaginal Swab Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	84
CT ATCC vr879 serovar H (EB/mL)	161

Two NG strains (ATCC 19424 and ATCC 49226) were tested. Replicates of 20 were evaluated at six concentrations. The LoD was estimated by probit analysis.

The LoD for NG, estimated by probit analysis, is 1.5 – 1.6 CFU/mL in a simulated swab matrix background (Table 4). An additional 30 NG strains were tested in a simulated matrix and the LoD was confirmed by testing replicates of three at or near the LoD.

Table 4: LoD of Two NG Strains in Pooled Vaginal Swab Matrix

Organism	LoD
NG ATCC19424 (CFU/mL)	1.5
NG ATCC49226 (CFU/mL)	1.6

Pooled Male Urine Matrix

Purified and titered elementary bodies from two CT serovars, ATCC vr885 serovar D and ATCC vr879 serovar H, were each tested in a sample matrix of negative pooled male urine. Replicates of 20 were evaluated at eight concentrations for CT serovar D and at seven concentrations for CT serovar H and LoDs were estimated by probit analysis. The claimed LoDs were confirmed by analyzing at least 20 replicate samples with elementary bodies diluted to the estimated LoD concentrations. For this study, the claimed LoD is defined as the lowest concentration at which 95% of at least 20 replicates are positive.

The claimed LoD for purified CT serovar D elementary bodies in male urine matrix is 75 EB/mL. The claimed LoD for purified CT serovar H elementary bodies in male urine matrix is 134 EB/mL (Table 5). In this study, LoDs for the remaining purified CT serovars (in EB/mL) are A (900), B (11), Ba (3037), C (34), E (12), F (151), G (48), I (43), J (112), K (88), LGV I (31), LGV II (40) and LGV III (157).

Table 5: LoD of Two CT Serovars in Pooled Male Urine Matrix

Organism	LoD
CT ATCC vr885 serovar D (EB/mL)	75
CT ATCC vr879 serovar H (EB/mL)	134

Two NG strains, ATCC 19424 and ATCC 49226, were tested in a sample matrix of negative pooled male urine. Replicates of 20 were evaluated at six concentrations. The LoD was estimated by probit analysis.

The LoD for NG, estimated by probit analysis, is 1.2 – 2. 7 CFU/mL in a male urine matrix background (Table 6). LoD for 30 additional NG strains was confirmed by testing replicates of three at or near the LoD.

Table 6: LoD of Two NG Strains in Pooled Male Urine Matrix

Organism	LoD
NG ATCC19424 (CFU/mL)	2.7
NG ATCC49226 (CFU/mL)	1.2

Analytical Specificity (Cross-reactivity)

One hundred and one (101) different microorganisms were tested at a concentration of at least 10^6 CFU/mL or 10^5 genome copies/mL in replicates of three (Table 7). All isolates were reported CT NOT DETECTED;NG NOT DETECTED; none of the organisms were detected by the Xpert CT/NG Assay. Positive and negative controls were included in the study. The analytical specificity was 100%.

Table 7: Analytical Specificity Determination for Xpert CT/NG Assay

Acinetobacter calcoaceticus	Herpes simplex virus I[1]	*Neisseria sicca (3)*
Acinetobacter lwoffi	Herpes simplex virus II[1]	*Neisseria subflava (2)*

Aerococcus viridans	Human papilloma virus[1]	*Paracoccus denitrificans*
Aeromonas hydrophila	*Kingella denitrificans*	*Peptostreptococcus anaerobius*
Alcaligenes faecalis	*Kingella kingae*	*Plesiomonas shigelloides*
Arcanobacterium pyogenes	*Klebsiella oxytoca*	*Propionibacterium acnes*
Bacteriodes fragilis	*Klebsiella pneumoniae*	*Proteus mirabilis*
Bifidobacterium adolescentis	*Lactobacillus acidophilus*	*Proteus vulgaris*
Branhamella catarrhalis	*Lactobacillus brevis*	*Providencia stuartii*
Brevibacterium linens	*Lactobacillus jensonii*	*Pseudomonas aeruginosa*
Candida albicans	*Lactobacillus lactis*	*Pseudomonas fluorescens*
Candida glabrata	*Legionella pneumophila*	*Pseudomonas putida*
Candida parapsilosis	*Leuconostoc paramensenteroides*	*Rahnella aquatilis*
Candida tropicalis	*Listeria monocytogenes*	*Saccharomyces cerevisiae*
Chlamydia pneumoniae	*Micrococcus luteus*	*Salmonella minnesota*
Chromobacterium violaceum	*Moraxella lacunata*	*Salmonella typhimurium*
Citrobacter freundii	*Moraxella osloensis*	*Serratia marcescens*
Clostridium perfringens	*Morganella morganii*	*Staphylococcus aureus*
Corynebacterium genitalium	*Mycobacterium smegmatis*	*Staphylococcus epidermidis*
Corynebacterium xerosis	*N. meningiditis*	*Staphylococcus saprophyticus*
Cryptococcus neoformans	*N. meningitidis Serogroup A*	*Streptococcus agalactiae*
Cytomegalovirus[1]	*N. meningitidis Serogroup B*	*Streptococcus bovis*
Eikenella corrodens	*N. meningitidis Serogroup C*	*Streptococcus mitis*
Entercoccus avium	*N. meningitidis Serogroup D*	*Streptococcus mutans*
Entercoccus faecalis	*N. meningitidis Serogroup W135*	*Streptococcus pneumoniae*
Entercoccus faecium	*N. meningitidis Serogroup Y*	*Streptococcus pyogenes*
Enterobacter aerogenes	*Neisseria cinerea*	*Streptococcus salivarius*
Enterobacter cloacae	*Neisseria dentrificans*	*Streptococcus sanguis*
Erysipelothrix rhusiopathiae	*Neisseria elongata (3)*	*Streptococcus griseinus*
Escherichia coli	*Neisseria flava*	*Vibrio parahaemolyticus*
Elizabethkingia meningoseptica[2]	*Neisseria flavescens (2)*	*Yersinia enterocolitica*
Fusobacterium nucleatum	*Neisseria lactamica (5)*	

Gardnerella vaginalis	*Neisseria mucosa (3)*	
Gemella haemolysans	*Neisseria perflava*	
Haemophilus influenzae	*Neisseria polysaccharea*	

(n) number of strains tested
[1] Tested at 1 x 10^5 genome copies/mL
[2] Previously known as *Flavobacterium meningosepticum*

Interfering Substances

Performance of the Xpert CT/NG Assay was evaluated in the presence of potentially interfering substances. The evaluated substances were diluted into vaginal/endocervical swab simulated matrix and urine matrix containing either 5x LoD CT serovar D and NG strain ATCC 49226 or x LoD CT serovar H and NG strain ATCC 19424.

There was no assay interference in the presence of the substances at the concentrations for vaginal/endocervical matrix (Table 8) and urine matrix (Table 9).

Table 8: Potentially Interfering Substances in Swab Matrix

Substance	Concentration
Blood	1.0% v/v
Mucin	0.8% w/v
Seminal Fluid	5.0% v/v
Hormones	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol
LGV II (CT EB)	10^6 EB/mL
Vagisil Anti Itch Cream	0.25% w/v
Clotrimazole Vaginal cream	0.25% w/v
Preparation H Hemorroidal cream	0.25% w/v
Miconazole 3	0.25% w/v
Monistat 1	0.25% w/v
Zovirax Cold Sore Cream	0.25% w/v
Vagisil Moisturizer	0.25% w/v
Vagi Gard Moisturizing Gel	0.25% w/v
KY Jelly Personal Lubricant	0.25% w/v

Substance	Concentration
Yeast Gard Douche	0.25% w/v
Delfen Vaginal Contraceptive Foam	0.25% w/v
VH Essentials Povidone-Iodine Medicated Douche	0.25% v/v
Leukocytes	10^6 cells/mL

Table 9: Potentially Interfering Substances in Urine Matrix

Substance	Concentration
Blood	0.3% v/v
Mucin	0.2% v/v
Seminal Fluid	5.0% v/v
Hormones	7 mg/mL Progesterone + 0.07 mg/mL Beta Estradiol
LGV II (CT EB)	10^6 EB/mL
Leukocytes	10^6 cells/mL
Norforms Deodorant Suppositories	0.25% w/v
BSA	10 mg/ml
Glucose	10 mg/mL
Bilirubin	0.2 mg/mL
Aspirin	40 mg/mL
Azithromycin	1.8 mg/mL
Doxycycline	3.6 mg/mL
Organisms - UTI Candida albicans/ Staphylococcus aureus/Escherichia coli	2.9 x 10^4 CFU/mL
Acetaminophen	3.2 mg/mL
Vagisil Feminine Powder	0.25% w/v
Acidic Urine	pH 4.0
Alkaline Urine	pH 9.0

Carry-Over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run following very high

positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a sample with high CT spike (1.9 x 10^4 EB/mL) and a high NG spike (5.2 x 10^5 CFU/mL). Two sample types were used for this testing: a) known pooled negative urine samples; and b) known pooled negative swab samples. Each sample type was tested in each of four GeneXpert modules for a total of 44 runs for both swab and urine samples resulting in 20 positives and 24 negatives. All 40 positive samples were correctly reported as CT DETECTED;NG DETECTED. All 48 negative samples were correctly reported as CT NOT DETECTED;NG NOT DETECTED.

Clinical Performance Characteristics:

Reproducibility

Reproducibility of the Xpert CT/NG Assay was evaluated at three sites using specimens comprised of CT and NG organisms seeded into pooled, negative male urine (urine matrix) or in pooled, negative female vaginal swab samples (swab matrix). The specimens were prepared at concentration levels representing low positive (1X LoD), moderate positive (2-3X LoD), and high positive (>20X LoD) for each organism. Negative panel members were also included, and were comprised of pooled, negative male urine and pooled, negative vaginal swab samples. A panel of 22 specimens (11 in urine matrix and 11 in swab matrix) was tested on five different days by two different operators four times per day at three sites (22 specimens x 2 operators/day x 5 days x 4 replicates per day x 3 sites). Three lots of Xpert CT/NG reagents were included in the study, with two lots being tested at each site. Xpert CT/NG Assays were performed according to the Xpert CT/NG Assay procedure. The rate of agreement with expected results of CT and NG for each panel member is presented in Tables 10 and 11.

Table 10: Summary of Reproducibility Results by Study Site; Percent Agreement Swab Samples

Sample		Site 1 (GeneXpert Dx)	Site 2 (Infinity-80)	Site 3 (Infinity-48)	% Total Agreement by Sample
CT >20X LoD; NG >20X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD; NG 1X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	87.5% (35/40)	97.5% (39/40)	95.0% (38/40)	93.3% (112/120)
CT >20X LoD; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD; NG >20X LoD	CT	90.0% (36/40)	97.5% (39/40)	95.0% (38/40)	94.2% (113/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD; NG 1X LoD	CT	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
	NG	92.5% (37/40)	90.0% (36/40)	90.0% (36/40)	90.8% (109/120)
CT 1X LoD; NG neg	CT	97.5% (39/40)	90.0% (36/40)	90.0% (36/40)	92.5% (111/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 2-3X LoD; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg; NG >20X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg; NG 1X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100.0% (40/40)	97.5% (39/40)	97.5% (39/40)	98.3% (118/120)
CT neg; NG 2-3X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
CT neg; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)

Table 11: Summary of Reproducibility Results by Study Site; Percent Agreement Urine Samples

Sample		Site 1 (GeneXpert Dx)	Site 2 (Infinity-80)	Site 3 (Infinity-48)	% Total Agreement by Sample
CT >20X LoD; NG >20X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT >20X LoD; NG 1X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	87.5% (35/40)	97.5% (39/40)	95.0% (38/40)	93.3% (112/120)
CT >20X LoD; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD; NG >20X LoD	CT	90.0% (36/40)	97.5% (39/40)	95.0% (38/40)	94.2% (113/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 1X LoD; NG 1X LoD	CT	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
	NG	92.5% (37/40)	90.0% (36/40)	90.0% (36/40)	90.8% (109/120)
CT 1X LoD; NG neg	CT	97.5% (39/40)	90.0% (36/40)	90.0% (36/40)	92.5% (111/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT 2-3X LoD; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg; NG >20X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
CT neg; NG 1X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100.0% (40/40)	97.5% (39/40)	97.5% (39/40)	98.3% (118/120)
CT neg; NG 2-3X LoD	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	97.5% (39/40)	100% (40/40)	100% (40/40)	99.2% (119/120)
CT neg; NG neg	CT	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)
	NG	100% (40/40)	100% (40/40)	100% (40/40)	100% (120/120)

The reproducibility of the Xpert CT/NG Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, and between-runs for each panel member are presented in Tables 12 through 14.

Table 12: Summary of Reproducibility data for Swab and Urine Specimens – CT1 Target

Type	Target Conc.					Between-Site		Between- Lot		Between-Day		Between-Run[1]		Within-Run		Total	
	CT (LoD)	NG (LoD)	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	120/120	100	20.67	0.21	1.0	0.11	0.5	0.11	0.5	0.00	0.0	0.29	1.4	0.39	1.9
	>20X	1X	112/120	93.3	20.73	0.29	1.4	0.37	1.8	0.00	0.0	0.00	0.0	1.59	7.7	1.66	8.0
	>20X	NEG	120/120	100	20.59	0.00	0.0	0.21	1.0	0.06	0.3	0.08	0.4	0.26	1.3	0.35	1.7
	1X	>20X	113/120	94.2	37.20	0.10	0.3	0.21	0.6	0.00	0.0	0.00	0.0	1.15	3.1	1.18	3.2
	1X	1X	106/120	88.3	37.04	0.17	0.5	0.00	0.0	0.00	0.0	0.12	0.3	1.08	2.9	1.10	3.0
	1X	NEG	111/120	92.5	37.04	0.06	0.2	0.00	0.0	0.00	0.0	0.00	0.0	1.12	3.0	1.12	3.0
	2-3X	NEG	120/120	100	35.63	0.13	0.4	0.00	0.0	0.15	0.4	0.10	0.3	0.77	2.2	0.80	2.3
	NEG	>20X	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	1X	118/120	98.3	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	2-3X	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	120/120	100	21.46	0.23	1.0	0.00	0.0	0.12	0.5	0.02	0.1	0.31	1.4	0.40	1.9
	>20X	1X	115/120	95.8	21.33	0.13	0.6	0.05	0.2	0.13	0.6	0.00	0.0	0.43	2.0	0.47	2.2
	>20X	NEG	120/120	100	21.36	0.19	0.9	0.00	0.0	0.12	0.6	0.02	0.1	0.47	2.2	0.52	2.4
	1X	>20X	111/120	92.5	37.24	0.36	1.0	0.00	0.0	0.00	0.0	0.00	0.0	1.33	3.6	1.38	3.7
	1X	1X	97/120	80.8	37.15	0.40	1.1	0.18	0.5	0.17	0.4	0.00	0.0	1.02	2.8	1.13	3.0
	1X	NEG	113/120	94.2	37.39	0.10	0.3	0.32	0.9	0.00	0.0	0.00	0.0	1.38	3.7	1.42	3.8
	2-3X	NEG	120/120	100	35.26	0.24	0.7	0.00	0.0	0.30	0.9	0.00	0.0	0.80	2.3	0.89	2.5
	NEG	>20X	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	1X	118/120	98.3	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	2-3X	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

[1]A run is defined as the four samples per panel member run by one operator at one site on one day

Table 13: Summary of Reproducibility data for Swab and Urine Specimens – NG2 Target

Type	Target Conc.					Between-Site		Between- Lot		Between-Day		Between-Run[1]		Within-Run		Total	
	CT (LoD)	NG (LoD)	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	120/120	100	19.65	0.03	0.1	0.09	0.4	0.07	0.3	0.02	0.1	0.24	1.2	0.26	1.3
	>20X	1X	112/120	93.3	35.38	0.22	0.6	0.00	0.0	0.00	0.0	0.00	0.0	1.98	5.6	1.99	5.6
	>20X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1X	>20X	113/120	94.2	19.69	0.12	0.6	0.00	0.0	0.19	1.0	0.00	0.0	0.43	2.2	0.49	2.5
	1X	1X	106/120	88.3	35.61	0.00	0.0	0.53	1.5	0.00	0.0	0.80	2.2	1.37	3.9	1.67	4.7
	1X	NEG	111/120	92.5	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	>20X	120/120	100	19.60	0.10	0.5	0.07	0.4	0.00	0.0	0.07	0.4	0.20	1.0	0.25	1.3
	NEG	1X	118/120	98.3	35.43	0.39	1.1	0.00	0.0	0.04	0.1	0.22	0.6	0.94	2.6	1.04	2.9
	NEG	2-3X	119/120	99.2	33.97	0.00	0.0	0.15	0.4	0.00	0.0	0.15	0.4	0.71	2.1	0.74	2.2
	NEG	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	120/120	100	20.34	0.06	0.3	0.09	0.4	0.00	0.0	0.07	0.3	0.23	1.1	0.26	1.3
	>20X	1X	115/120	95.8	35.41	0.00	0.0	0.00	0.0	0.19	0.5	0.30	0.8	1.15	3.3	1.20	3.4
	>20X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1X	>20X	111/120	92.5	20.40	0.06	0.3	0.07	0.3	0.00	0.0	0.00	0.0	0.39	1.9	0.40	2.0
	1X	1X	97/120	80.8	35.57	0.20	0.6	0.00	0.0	0.13	0.4	0.10	0.3	1.28	3.6	1.31	3.7
	1X	NEG	113/120	94.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	>20X	119/120	99.2	20.39	0.00	0.0	0.07	0.4	0.14	0.7	0.05	0.3	0.26	1.3	0.31	1.5
	NEG	1X	118/120	98.3	35.35	0.00	0.0	0.11	0.3	0.00	0.0	0.36	1.0	0.92	2.6	0.99	2.8
	NEG	2-3X	120/120	100	33.80	0.00	0.0	0.18	0.5	0.00	0.0	0.00	0.0	0.54	1.6	0.57	1.7
	NEG	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

[1]A run is defined as the four samples per panel member run by one operator at one site on one day

Table 14: Summary of Reproducibility data for Swab and Urine Specimens – NG4 Target

Type	Target Conc.					Between-Site		Between- Lot		Between-Day		Between-Run[1]		Within-Run		Total	
	CT (LoD)	NG (LoD)	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	120/120	100	19.34	0.00	0.0	0.12	0.6	0.11	0.6	0.00	0.0	0.39	2.0	0.42	2.2
	>20X	1X	112/120	93.3	35.00	0.41	1.2	0.00	0.0	0.00	0.0	0.32	0.9	1.89	5.4	1.96	5.6
	>20X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1X	>20X	113/120	94.2	19.41	0.07	0.4	0.00	0.0	0.14	0.7	0.03	0.2	0.49	2.5	0.52	2.7
	1X	1X	106/120	88.3	35.47	0.32	0.9	0.00	0.0	0.00	0.0	0.70	2.0	0.90	2.5	1.19	3.3
	1X	NEG	111/120	92.5	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	>20X	120/120	100	19.35	0.02	0.1	0.04	0.2	0.00	0.0	0.07	0.4	0.28	1.5	0.29	1.5
	NEG	1X	118/120	98.3	35.05	0.00	0.0	0.16	0.5	0.00	0.0	0.00	0.0	1.00	2.9	1.01	2.9
	NEG	2-3X	119/120	99.2	33.57	0.14	0.4	0.17	0.5	0.00	0.0	0.00	0.0	0.78	2.3	0.81	2.4
	NEG	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	120/120	100	20.06	0.12	0.6	0.12	0.6	0.09	0.4	0.00	0.0	0.39	1.9	0.43	2.1
	>20X	1X	115/120	95.8	35.27	0.17	0.5	0.13	0.4	0.00	0.0	0.00	0.0	1.04	2.9	1.06	3.0
	>20X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1X	>20X	111/120	92.5	20.16	0.00	0.0	0.08	0.4	0.00	0.0	0.12	0.6	0.56	2.8	0.58	2.9
	1X	1X	97/120	80.8	35.25	0.00	0.0	0.00	0.0	0.41	1.2	0.00	0.0	1.17	3.3	1.24	3.5
	1X	NEG	113/120	94.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	NEG	120/120	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	>20X	119/120	99.2	20.12	0.09	0.5	0.10	0.5	0.06	0.3	0.00	0.0	0.41	2.0	0.43	2.2
	NEG	1X	118/120	98.3	35.05	0.24	0.7	0.00	0.0	0.15	0.4	0.12	0.4	1.09	3.1	1.13	3.2
	NEG	2-3X	120/120	100	33.67	0.00	0.0	0.33	1.0	0.00	0.0	0.16	0.5	0.83	2.5	0.91	2.7
	NEG	NEG	119/120	99.2	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation. N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.[1]A run is defined as the four samples per panel member run by one operator at one site on one day

Instrument System Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the Infinity-80 Instrument Systems using specimens comprised of CT and NG organisms seeded into negative urine (urine matrix) or diluent for the Xpert CT/NG Assay (swab matrix). The specimens were prepared at concentration levels representing low positive (0.25-0.5X LoD), moderate positive (2-3X LoD), and high positive (>20X LoD) for each organism. Negative panel members were also included and were comprised of negative urine and negative diluent. A panel of 20 specimens (10 in urine matrix and 10 in swab matrix) was tested on 12 different days by two operators. Each operator conducted four runs of each panel specimen per day on each of the two instrument systems (20 specimens x 4 times/ day x 12 days x 2 operators x 2 instrument systems). One lot of Xpert CT/NG Assay was used for the study. Xpert CT/NG assays were performed according to the Xpert CT/NG Assay procedure. The rate of agreement with expected results of CT and NG for each panel member is presented by instrument in Tables 15 and 16.

Table 15: Summary of Instrument System Precision Results; Percent Agreement Swab Matrix

Sample		GeneXpert Dx	Infinity-80	% Total Agreement by Sample
CT >20X LoD; NG >20X LoD	CT	100% (96/96)	100% (95/95)[a]	100% (191/191)
	NG	100% (96/96)	100% (95/95)[a]	100% (191/191)
CT >20X LoD; NG 0.25-0.5X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	62.5% (60/96)	52.1% (50/96)	57.3% (110/192)
CT >20X LoD; NG neg	CT	100% (96/96)	100% (95/95)[b]	100% (191/191)
	NG	100% (96/96)	100% (95/95)[b]	100% (191/191)
CT 0.25-0.5X LoD; NG >20X LoD	CT	46.9% (45/96)	42.7% (41/96)	44.8% (86/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT 0.25-0.5X LoD; NG 0.25-0.5X LoD	CT	55.2% (53/96)	60.4% (58/96)	57.8% (111/192)
	NG	50.0% (48/96)	66.7% (64/96)	58.3% (112/192)
CT 0.25-0.5X LoD; NG neg	CT	61.5% (59/96)	62.1% (59/95)[c]	61.8% (118/191)
	NG	100% (96/96)	100% (95/95)[c]	100% (191/191)
CT 2-3X LoD; NG 2-3X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT neg; NG >20X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT neg; NG 0.25-0.5X LoD	CT	100% (95/95)[b]	100% (96/96)	100% (191/191)
	NG	58.9% (56/95)[b]	62.5% (60/96)	60.7% (116/191)
CT neg; NG neg	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)

[a]One sample was indeterminate after initial and retest.
[b]One sample each of CT >20X LoD; NG neg sample and CT neg; NG 0.25-0.5X LoD resulted in ERROR on initial test and were not retested.
[c]One sample mistakenly not tested.

Table 16: Summary of Instrument System Precision Results; Percent Agreement Urine Matrix

Sample		GeneXpert Dx	Infinity-80	% Total Agreement by Sample
CT >20X LoD; NG >20X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT >20X LoD; NG 0.25-0.5X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	46.9% (45/96)	49.0% (47/96)	47.9% (92/192)
CT >20X LoD; NG neg	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT 0.25-0.5X LoD; NG >20X LoD	CT	50.0% (48/96)	52.1% (50/96)	51.0% (98/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT 0.25-0.5X LoD; NG 0.25-0.5X LoD	CT	44.8% (43/96)	39.6% (38/96)	42.2% (81/192)
	NG	62.5% (60/96)	58.3% (56/96)	60.4% (116/192)
CT 0.25-0.5X LoD; NG neg	CT	46.9% (45/96)	46.9% (45/96)	46.9% (90/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT 2-3X LoD; NG 2-3X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT neg; NG >20X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)
CT neg; NG 0.25-0.5X LoD	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	36.5% (35/96)	33.3% (32/96)	34.9% (67/192)
CT neg; NG neg	CT	100% (96/96)	100% (96/96)	100% (192/192)
	NG	100% (96/96)	100% (96/96)	100% (192/192)

The reproducibility of the Xpert CT/NG Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-instruments, between-days, and between-runs for each panel member are presented in Tables 17 through 19.

Table 17: Summary of Reproducibility data for Swab and Urine Specimens – CT1 Target

Type	Target Conc.					Between-Instrument		Between-Day		Between-Run[1]		Within-Run		Total	
	CT	NG	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	191/191	100	23.52	0.05	0.2	0.02	0.1	0.00	0.0	0.25	1.1	0.26	1.1
	>20X	0.25-0.5X	110/192	57.3	23.52	0.00	0.0	0.00	0.0	0.08	0.3	0.18	0.7	0.19	0.8
	>20X	NEG	191/191	100	23.55	0.03	0.1	0.00	0.0	0.00	0.0	0.22	0.9	0.22	0.9
	0.25-0.5X	>20X	86/192	44.8	38.77	0.00	0.0	0.00	0.0	0.32	0.8	1.38	3.6	1.42	3.7
	0.25-0.5X	0.25-0.5X	59/192	30.7	38.46	0.00	0.0	0.30	0.8	0.00	0.0	1.35	3.5	1.39	3.6
	0.25-0.5X	NEG	118/191	61.8	38.05	0.08	0.2	0.00	0.0	0.00	0.0	1.26	3.3	1.26	3.3
	2-3X	2-3X	192/192	100	31.49	0.04	0.1	0.00	0.0	0.06	0.2	0.24	0.8	0.25	0.8
	NEG	>20X	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	0.25-0.5X	116/191	60.7	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	192/192	100	24.35	0.05	0.2	0.20	0.8	0.10	0.4	0.30	1.2	0.38	1.6
	>20X	0.25-0.5X	92/192	47.9	24.25	0.00	0.0	0.06	0.3	0.00	0.0	0.62	2.6	0.62	2.6
	>20X	NEG	192/192	100	24.12	0.00	0.0	0.15	0.6	0.19	0.8	0.34	1.4	0.41	1.7
	0.25-0.5X	>20X	98/192	51.0	38.33	0.12	0.3	0.00	0.0	0.84	2.2	1.03	2.7	1.33	3.5
	0.25-0.5X	0.25-0.5X	48/192	25.0	38.26	0.00	0.0	0.00	0.0	0.56	1.5	1.05	2.7	1.19	3.1
	0.25-0.5X	NEG	90/192	46.9	38.39	0.00	0.0	0.00	0.0	0.00	0.0	1.09	2.8	1.09	2.8
	2-3X	2-3X	192/192	100	31.85	0.00	0.0	0.11	0.4	0.18	0.6	0.32	1.0	0.39	1.2
	NEG	>20X	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	0.25-0.5X	67/192	34.9	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

Table 18: Summary of Reproducibility data for Swab and Urine Specimens – NG2 Target

Type	Target Conc.					Between-Instrument		Between-Day		Between-Run[1]		Within-Run		Total	
	CT	NG	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	191/191	100	19.03	0.01	0.0	0.02	0.1	0.00	0.0	0.21	1.1	0.21	1.1
	>20X	0.25-0.5X	110/192	57.3	37.63	0.07	0.2	0.46	1.2	0.00	0.0	1.55	4.1	1.62	4.3
	>20X	NEG	191/191	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	0.25-0.5X	>20X	86/192	44.8	19.08	0.00	0.0	0.00	0.0	0.10	0.5	0.31	1.6	0.32	1.7
	0.25-0.5X	0.25-0.5X	59/192	30.7	36.78	0.00	0.0	0.24	0.6	0.00	0.0	1.47	4.0	1.49	4.0
	0.25-0.5X	NEG	118/191	61.8	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	2-3X	192/192	100	31.35	0.00	0.0	0.00	0.0	0.00	0.0	0.33	1.1	0.33	1.1
	NEG	>20X	192/192	100	19.02	0.00	0.0	0.00	0.0	0.07	0.4	0.22	1.2	0.23	1.2
	NEG	0.25-0.5X	116/191	60.7	36.77	0.00	0.0	0.46	1.2	0.00	0.0	1.65	4.5	1.71	4.7
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	192/192	100	19.85	0.00	0.0	0.15	0.7	0.00	0.0	0.34	1.7	0.37	1.8
	>20X	0.25-0.5X	92/192	47.9	36.72	0.15	0.4	0.00	0	0.00	0.0	1.36	3.7	1.37	3.7
	>20X	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	0.25-0.5X	>20X	98/192	51.0	19.51	0.00	0.0	0.00	0.0	0.00	0.0	1.20	6.1	1.20	6.1
	0.25-0.5X	0.25-0.5X	48/192	25.0	36.38	0.26	0.7	0.00	0.0	1.98	5.5	1.13	3.1	2.30	6.3
	0.25-0.5X	NEG	90/192	46.9	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	2-3X	192/192	100	31.53	0.00	0.0	0.09	0.3	0.16	0.5	0.42	1.3	0.46	1.4
	NEG	>20X	192/192	100	19.26	0.14	0.7	0.00	0.0	0.17	0.9	0.43	2.3	0.49	2.4
	NEG	0.25-0.5X	67/192	34.9	36.88	0.00	0.0	0.31	0.8	0.00	0	1.45	3.9	1.48	7.5
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

Table 19: Summary of Reproducibility data for Swab and Urine Specimens – NG4 Target

Type	Target Conc.					Between-Instrument		Between-Day		Between-Run[1]		Within-Run		Total	
	CT	NG	Agree/N	Agrmt (%)	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Swab	>20X	>20X	191/191	100	18.67	0.00	0.0	0.00	0.0	0.19	1.0	0.34	1.8	0.39	2.1
	>20X	0.25-0.5X	110/192	57.3	36.94	0.49	1.3	0.00	0.0	0.10	0.3	1.63	4.4	1.71	4.6
	>20X	NEG	191/191	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	0.25-0.5X	>20X	86/192	44.8	18.72	0.06	0.3	0.00	0.0	0.21	1.1	0.41	2.2	0.46	2.5
	0.25-0.5X	0.25-0.5X	59/192	30.7	36.57	0.00	0.0	0.50	1.4	0.00	0.0	1.55	4.3	1.63	4.5
	0.25-0.5X	NEG	118/191	61.8	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	2-3X	192/192	100	31.06	0.00	0.0	0.05	0.2	0.00	0.0	0.42	1.4	0.43	1.4
	NEG	>20X	192/192	100	18.69	0.00	0.0	0.00	0.0	0.22	1.2	0.38	2.0	0.44	2.3
	NEG	0.25-0.5X	116/191	60.7	36.31	0.08	0.2	0.13	0.4	0.00	0.0	1.24	3.4	1.25	3.4
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Urine	>20X	>20X	192/192	100	19.44	0.01	0.1	0.10	0.5	0	0	0.45	2.3	0.46	2.4
	>20X	0.25-0.5X	92/192	47.9	36.31	0	0	0.04	0.1	0.17	0.5	1.18	3.2	1.19	6.1
	>20X	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	0.25-0.5X	>20X	98/192	51.0	19.08	0	0	0	0	0	0	1.35	7.1	1.35	6.9
	0.25-0.5X	0.25-0.5X	48/192	25.0	36.16	0	0	0.24	0.7	0	0	1.98	5.5	2.00	10.3
	0.25-0.5X	NEG	90/192	46.9	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2-3X	2-3X	192/192	100	31.09	0	0	0.16	0.5	0.11	0.4	0.49	1.6	0.53	2.7
	NEG	>20X	192/192	100	18.80	0.04	0.2	0	0	0.14	0.7	0.47	2.5	0.50	2.6
	NEG	0.25-0.5X	67/192	34.9	36.58	0.18	0.5	0	0	0.74	2.0	1.40	3.8	1.60	8.2
	NEG	NEG	192/192	100	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Agrmt=Agreement, Conc=concentration, CV=coefficient of variation, N/A=Not Applicable for negative samples, SD=standard deviation

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

Clinical Performance Study

Performance characteristics of the Xpert CT/NG Assay were determined in a multi-site prospective investigational study at 36 US and UK institutions by comparing the Xpert CT/NG Assay to a patient infected status (PIS) algorithm based on combined results from two currently marketed NAAT tests.

Study participants included consenting asymptomatic and symptomatic, sexually active males and females seen at locations including, but not limited to: OB/GYN, sexually transmitted disease (STD), teen, public health, and family planning clinics. The average age among female study participants was 30.3 years (range = 14 to 83 years); the average age among male study participants was 37.7 years (range = 17 to 74 years).

The study specimens consisted of prospectively collected male urine, female urine, endocervical swabs, urethral swabs and patient-collected vaginal swabs (collected in a clinical setting).

A female study participant was categorized as infected (I) by PIS for CT or NG if at least one positive result was reported from each reference NAAT test. If both NAAT tests resulted in equivocal results for both sample types (swab and urine) the PIS status was defined as equivocal (EQ). This is the only scenario for an overall PIS of EQ; no study participants fell into this category for this study. Female study participants with positive results on both reference urine specimens and negative results on both reference swab specimens were categorized as infected (I) for urine and not infected (NI) for the swab specimen. Any other combination of results was categorized as not infected (NI).

A male study participant was categorized as infected (I) by PIS for CT or NG if at least one positive result was reported from each reference NAAT test. If both NAAT tests resulted in equivocal results for both sample types (swab and urine) the PIS status was defined as equivocal (EQ). This is the only scenario for an overall PIS of EQ; no study participants fell into this category for this study. Any other combination of results was categorized as not infected (NI).

Performance of the Xpert CT/NG Assay was calculated relative to the PIS for each of the three female sample types (endocervical swabs, self-collected vaginal swabs and urine), and male urine.

During the clinical evaluation of the Xpert CT/NG Assay, a total of 212 female subjects were infected with CT. Symptoms were reported in 41.0% (87/212) of infected and 34.1% (1221/3579) non-infected female subjects. A total of 54 female subjects were infected with NG. Symptoms were reported in 53.7% (29/54) of infected and 34.1% (1273/3729) non-infected female subjects. A total of 196 male subjects were infected with CT. Symptoms were reported in 62.8% (123/196) of infected and 18.0% (584/3248) non-infected male subjects. A total of 119 male subjects were infected with NG. Symptoms were reported in 89.1% (106/119) of infected and 18.1% (601/3325) non-infected male subjects.

Among the 14,790 tests performed, 416 had to be retested due to ERROR, INVALID or NO RESULT outcomes (2.81%, 95% CI 2.56-3.09). Of those, 355 specimens yielded valid results upon repeat assay (18 specimens were not retested). The overall valid reporting rate of the assay was 99.6% (14,729/14,790).

Chlamydia trachomatis Performance Results

Results from the Xpert CT/NG Assay were compared to the patient infected status (PIS) algorithm for determination of sensitivity, specificity, and predictive values. Sensitivity and specificity for CT by gender, specimen type, and symptom status are presented in Table 20.

Table 20: Xpert CT/NG Assay vs. Patient Infected Status for CT Detection

Specimen		Sx Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95 CI)	Specificity % (95 CI)	PPV % (95 CI)	NPV % (95 CI)
Female	PC-VS	Sym	1294	79	20	1195	0	6.1	100 (95.4-100)	98.4 (97.5-99.0)	79.8 (70.5-87.2)	100 (99.7-100)
		Asym	2472	121	11	2339	1	4.9	99.2 (95.5-100)	99.5 (99.2-99.8)	91.7 (85.6-95.8)	>99.9 (99.8-100)
		All	3766	200	31	3534	1	5.3	99.5 (97.3-100)	99.1 (98.8-99.4)	86.6 (81.5-90.7)	>99.9 (99.8-100)
	ES	Sym	1293	76	5	1209	3	6.1	96.2 (89.3-99.2)	99.6 (99.0-99.9)	93.8 (86.2-98.0)	99.8 (99.3-99.9)
		Asym	2464	117	11	2331	5	5.0	95.9 (90.7-98.7)	99.5 (99.2-99.8)	91.4 (85.1-95.6)	99.8 (99.5-99.9)
		All	3757	193	16	3540	8	5.4	96.0 (92.3-98.3)	99.6 (99.3-99.7)	92.3 (87.9-95.6)	99.8 (99.6-99.9)
	Urine	Sym	1292	84	4	1203	1	6.6	98.8 (93.6-100)	99.7 (99.2-99.9)	95.5 (88.8-98.7)	99.9 (99.5-100)
		Asym	2475	123	2	2347	3	5.1	97.6 (93.2-99.5)	99.9 (99.7-100)	98.4 (94.3-99.8)	99.9 (99.6-100)
		All	3767	207	6	3550	4	5.6	98.1 (95.2-99.5)	99.8 (99.6-99.9)	97.2 (94.0-99.0)	99.9 (99.7-100)
Male	Urine	Sym	706	120	2	581	3	17.4	97.6 (93.0-99.5)	99.7 (98.8-100)	98.4 (94.2-99.8)	99.5 (98.5-99.9)
		Asym	2730	73	5	2652	0	2.7	100.0 (95.1-100)	99.8 (99.6-99.9)	93.6 (85.7-97.9)	100 (99.9-100)
		All	3436	193	7	3233	3	5.7	98.5 (95.6-99.7)	99.8 (99.6-99.9)	96.5 (92.9-98.6)	99.9 (99.7-100)

TP=true positive, FP=false positive, TN=true negative, FN=false negative, ES=endocervical swab, PC-VS=patient-collected vaginal swab

Neisseria gonorrhoeae Performance Results

Results from the Xpert CT/NG Assay were compared to the patient infected status (PIS) algorithm for determination of sensitivity, specificity, and predictive values. Sensitivity and specificity for NG by gender, specimen type, and symptom status are presented in Table 21.

Table 21: Xpert CT/NG Assay vs. Patient Infected Status for NG Detection

Specimen		Sx Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95 CI)	Specificity % (95 CI)	PPV % (95 CI)	NPV % (95 CI)
Female	PC-VS	Sym	1294	27	2	1265	0	2.1	100 (87.2-100)	99.8 (99.4-100)	93.1 (77.2-99.2)	100 (99.7-100)
		Asym	2472	25	1	2446	0	1.0	100 (86.3-100)	>99.9 (99.8-100)	96.2 (80.4-99.9)	100 (99.8-100)
		All	3766	52	3	3711	0	1.4	100 (93.2-100)	99.9 (99.8-100)	94.5 (84.9-98.9)	100 (99.9-100)
	ES	Sym	1293	27	1	1265	0	2.1	100 (87.2-100)	99.9 (99.6-100)	96.4 (81.7-99.9)	100 (99.7-100)
		Asym	2464	25	0	2439	0	1.0	100 (86.3-100)	100 (99.8-100)	100 (86.3-100)	100 (99.8-100)
		All	3757	52	1	3704	0	1.4	100 (93.2-100)	>99.9 (99.8-100)	98.1 (89.9-100)	100 (99.9-100)
	Urine	Sym	1292	28	0	1263	1	2.2	96.6 (82.2-99.9)	100 (99.7-100)	100 (87.7-100)	99.9 (99.6-100)
		Asym	2475	23	1	2449	2	1.0	92.0 (74.0-99.0)	>99.9 (99.8-100)	95.8 (78.9-99.9)	99.9 (99.7-100)
		All	3767	51	1	3712	3	1.4	94.4 (84.6-98.8)	>99.9 (99.9-100)	98.1 (89.7-100)	99.9 (99.8-100)
Male	Urine	Sym	706	105	0	600	1	15.0	99.1 (94.9-100)	100 (99.4-100)	100 (96.5-100)	99.8 (99.1-100)
		Asym	2730	12	3	2714	1	0.5	92.3 (64.0-99.8)	99.9 (99.7-100)	80.0 (51.9-95.7)	>99.9 (99.8-100)
		All	3436	117	3	3314	2	3.5	98.3 (94.1-99.8)	99.9 (99.7-100)	97.5 (92.9-99.5)	99.9 (99.8-100)

TP=true positive, FP=false positive, TN=true negative, FN=false negative, ES=endocervical swab, PC-VS=patient-collected vaginal swab

Table 22 shows the number of results from symptomatic and asymptomatic females designated as infected or not infected with CT based on the PIS algorithm.

Table 22: Patient Infected Status – Female CT

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	-	-	1160	2269	3429
NI	-	-	-	-	IND	-	-	6	8	14
NI	-	-	-	-	-	IND[c]	-	6	16	22
NI	-	-	-	-	-	-	IND	5	6	11
NI	-	-	-	-	+	+	-	0	1	1
NI	-	-	-	-	+	-	-	6	4	10
NI	-	-	-	-	-	+	-	3	5	8
NI	-	-	-	-	-	-	+	1	0	1
NI	-	-	-	EQ[d]	-	-	-	6	20	26
NI	-	-	-	EQ	IND	IND	-	1	0	1
NI	-	-	EQ	-	-	-	-	3	4	7
NI	-	-	EQ	-	-	-	IND	1	0	1
NI	-	-	-	+	-	-	-	0	7	7
NI	-	-	+	-	-	-	-	3	0	3
NI	-	-	+	-	-	+	-	0	1	1
NI[f]	-	+	-	+	+	-	+	7	1	8
NI[f]	-	+	-	+	+	-	-	0	1	1
NI[f]	-	+	-	+	-	-	+	0	1	1
NI	-	+	-	-	-	-	-	1	0	1
NI	-	+	-	-	+	-	+	1	0	1
NI	+	-	-	-	-	-	-	4	8	12
NI	+	-	-	-	+	-	-	2	1	3
NI	+	-	-	-	+	+	-	1	2	3
NI	+	-	-	-	-	+	-	0	1	1
NI	+	+	-	-	-	-	-	1	0	1
NI	+	+	-	-	-	-	+	0	1	1
NI	+	+	-	-	+	+	+	1	1	2
NI	+	+	-	-	+	-	+	1	0	1
NI	+	+	-	-	+	-	-	1	0	1
Total Non-Infected								1221	2358	3579
I[e]	+	+	+	+	+	+	+	65	104	169
I	+	+	+	+	IND	+	+	0	1	1
I	+	+	+	+	+	IND	+	0	1	1
I	+	+	+	+	+	+	IND	1	0	1
I	+	+	+	+	-	+	+	0	1	1
I	+	+	+	+	+	-	+	0	1	1
I[f]	-	+	-	+	+	-	+	7	1	8
I[f]	-	+	-	+	+	-	-	0	1	1
I[f]	-	+	-	+	-	-	+	0	1	1
I	-	+	+	+	+	+	+	0	2	2
I	+	-	+	+	+	+	+	1	0	1
I	+	-	+	+	+	-	+	0	1	1
I	+	-	+	+	+	+	+	1	0	1
I	+	+	-	+	+	-	+	3	2	5
I	+	+	-	+	+	+	+	4	2	6

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
I	+	+	+	-	+	+	+	3	4	7
I	+	+	+	-	+	+	-	1	1	2
I	+	+	+	-	+	-	+	0	1	1
I	+	-	+	-	+	+	+	1	0	1
I	+	-	EQ	+	+	+	+	0	1	1
Total Infected								87	125	212

[a]PIS = Patient Infected Status; SW = Swab; UR = urine; PC-VS = Patient-collected Vaginal Swab; ES = Endocervical Swab
[b]NI = Non-infected
[c]IND = Indeterminate – ERROR, INVALID or NO RESULT by Xpert CT/NG Assay; specimens with IND results by Xpert are not included in the 2x2 tables for that specimen type.
[d]EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
[e]I = Infected
[f]These samples are infected for urine and non-infected for swabs. In this table they appear twice.

Table 23 shows the number of results from symptomatic and asymptomatic females designated as infected or not infected with NG based on the PIS algorithm.

Table 23: Patient Infected Status – Female NG

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	-	-	1229	2390	3619
NI	-	-	-	-	IND[c]	-	-	6	9	15
NI	-	-	-	-	-	IND	-	6	17	23
NI	-	-	-	-	-	-	IND	6	6	12
NI	-	-	-	-	+	-	+	0	1	1
NI	-	-	-	-	+	-	-	1	0	1
NI	-	-	EQ[d]	-	-	-	-	2	5	7
NI	-	-	-	EQ	-	-	-	9	20	29
NI	-	-	-	+	-	-	-	1	3	4
NI	-	-	+	-	-	-	-	7	4	11
NI[f]	-	+	-	+	+	+	+	1	0	1
NI[f]	-	+	-	+	-	-	+	1	0	1
NI	-	-	+	+	-	-	-	1	0	1
NI	+	-	-	-	-	-	-	1	1	2
NI	-	-	EQ	-	-	-	IND	1	0	1
NI	-	-	-	EQ	-	IND	IND	1	0	1
Total Non-Infected								1273	2456	3729
I[e]	+	+	+	+	+	+	+	19	19	38
I	+	+	+	-	+	+	+	2	2	4
I	+	-	+	+	+	+	+	1	1	2
I[f]	-	+	-	+	+	+	+	1	0	1
I[f]	-	+	-	+	-	-	+	1	0	1
I	+	-	+	-	+	+	-	1	2	3
I	+	-	+	-	+	+	+	1	0	1
I	+	+	-	+	+	+	+	1	0	1
I	+	+	+	EQ	+	+	+	0	1	1
I	+	+	EQ	+	+	+	+	1	0	1

PIS[a]	NAAT1		NAAT2		Xpert			Symptom Status		Total
	SW[a]	UR[a]	SW	UR	PC-VS[a]	ES[a]	UR	Symp	Asymp	
I	+	EQ	+	-	+	+	+	1	0	1
Total Infected								29	25	54

[a]PIS = Patient Infected Status; SW = Swab; UR = urine; PC-VS = Patient-collected Vaginal Swab; ES = Endocervical Swab
[b]NI = Non-infected
[c]IND = Indeterminate – ERROR, INVALID or NO RESULT by Xpert CT/NG Assay; specimens with IND results by Xpert are not included in the 2x2 tables for that specimen type.
[d]EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
[e]I = Infected
[f]These samples are infected for urine and non-infected for swabs. In this table they appear twice.

Table 24 shows the number of results from symptomatic and asymptomatic males designated as infected or not infected with CT based on the PIS algorithm.

Table 24: Patient Infected Status – Male CT

PIS[a]	NAAT1		NAAT2		GX	Symptom Status		Total
	SW[a]	UR[a]	SW	UR	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	568	2621	3189
NI	-	-	-	EQ[c]	-	0	19	19
NI	-	-	+	-	-	2	1	3
NI	+	-	-	-	-	6	1	7
NI	+	+	-	-	-	1	1	2
NI	-	-	-	+	-	2	7	9
NI	-	+	-	-	-	2	1	3
NI	-	-	EQ	-	-	0	1	1
NI	+	+	-	-	+	2	4	6
NI	-	-	-	-	+	0	1	1
NI	-	-	-	-	IND[d]	1	6	7
NI	-	-	-	EQ	IND	0	1	1
Total Non-Infected						584	2664	3248
I[e]	+	+	+	+	+	104	50	154
I	+	+	-	+	+	8	10	18
I	-	+	-	+	+	4	7	11
I	+	+	+	-	+	2	2	4
I	+	-	+	-	+	1	0	1
I	+	-	-	+	+	1	0	1
I	-	+	+	+	+	0	1	1
I	+	+	+	EQ	+	0	2	2
I	EQ	+	-	+	+	0	1	1
I	+	-	+	-	-	2	0	2
I	+	+	+	-	-	1	0	1
Total Infected						123	73	196

[a]PIS = Patient Infected Status; SW = Swab; UR = urine.
[b]NI = Non-infected
[c]EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
[d]IND = Indeterminate – ERROR, INVALID or NO RESULT by Xpert CT/NG Assay; specimens with IND results by Xpert are not included in the 2x2 tables for that specimen type.
[e]I = Infected

Table 25 shows the number of results from symptomatic and asymptomatic males designated as infected or not infected with NG based on the PIS algorithm

Table 25: Patient Infected Status – Male NG

PIS[a]	NAAT1		NAAT2		GX	Symptom Status		Total
	SW[a]	UR[a]	SW	UR	UR	Symp	Asymp	
NI[b]	-	-	-	-	-	597	2680	3277
NI	-	-	-	EQ[c]	-	0	21	21
NI	-	-	EQ	-	-	0	1	1
NI	EQ	EQ	-	-	-	1	0	1
NI	-	-	+	-	-	0	3	3
NI	-	-	-	+	-	0	3	3
NI	-	+	-	-	-	0	1	1
NI	+	-	-	-	-	2	5	7
NI	-	EQ	-	-	+	0	1	1
NI	EQ	-	+	-	+	0	1	1
NI	-	-	-	-	+	0	1	1
NI	-	-	-	-	IND[d]	1	6	7
NI	-	-	-	EQ	IND	0	1	1
Total Non-Infected						601	2724	3325
I[e]	+	+	+	+	+	105	11	116
I	+	+	+	-	+	0	1	1
I	+	-	+	-	-	0	1	1
I	+	-	-	+	-	1	0	1
Total Infected						106	13	119

[a]PIS = Patient Infected Status; SW = Swab; UR = urine.
[b]NI = Non-infected
[c]EQ = Equivocal result for this individual specimen type only; PIS status determined based on remaining specimens.
[d]IND = Indeterminate – ERROR, INVALID or NO RESULT by Xpert CT/NG Assay; specimens with IND results by Xpert are not included in the 2x2 tables for that specimen type.
[e]I = Infected

Hypothetical estimated positive and negative predictive values (PPV and NPV) for different prevalence rates using Xpert CT/NG Assay are shown in Tables 26 through 29 below. These calculations are based on a hypothetical prevalence and the overall sensitivity and specificity (compared to the patient infected status) observed during the Xpert CT/NG for a multi-center clinical study (Tables 20 and 21).

In patient-collected vaginal swab specimens, the overall sensitivity and specificity for CT were 99.5% and 99.1%, respectively (Table 20). The overall sensitivity and specificity for NG were 100% and 99.9%, respectively (Table 21). The following table shows PPV and NPV for patient-collected vaginal swab specimens using hypothetical prevalence rates.

Table 26: Hypothetical PPV and NPV– Patient-collected Vaginal Swabs

Prevalence Rate (%)	CT				NG			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	99.5	99.1	53.6	100	100	99.9	92.6	100
2	99.5	99.1	70.0	100	100	99.9	96.2	100
5	99.5	99.1	85.8	100	100	99.9	98.5	100
10	99.5	99.1	92.7	99.9	100	99.9	99.3	100
15	99.5	99.1	95.3	99.9	100	99.9	99.5	100
20	99.5	99.1	96.6	99.9	100	99.9	99.7	100
25	99.5	99.1	97.4	99.8	100	99.9	99.8	100
30	99.5	99.1	98.0	99.8	100	99.9	99.8	100
50	99.5	99.1	99.1	99.5	100	99.9	99.9	100

In endocervical swab specimens, the overall sensitivity and specificity for CT were 96.0% and 99.6%, respectively (Table 20). The overall sensitivity and specificity for NG were 100% and >99.9%, respectively (Table 21). The following table shows PPV and NPV for endocervical swab specimens using hypothetical prevalence rates.

Table 27: Hypothetical PPV and NPV– Endocervical Swabs

Prevalence Rate (%)	CT				NG			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	96.0	99.6	68.3	100	100	>99.9	97.4	100
2	96.0	99.6	81.3	99.9	100	>99.9	98.7	100
5	96.0	99.6	91.8	99.8	100	>99.9	99.5	100
10	96.0	99.6	96.0	99.6	100	>99.9	99.8	100
15	96.0	99.6	97.4	99.3	100	>99.9	99.8	100
20	96.0	99.6	98.2	99.0	100	>99.9	99.9	100
25	96.0	99.6	98.6	98.7	100	>99.9	99.9	100
30	96.0	99.6	98.9	98.3	100	>99.9	99.9	100
50	96.0	99.6	99.5	96.2	100	>99.9	100	100

In female urine specimens, the overall sensitivity and specificity for CT were 98.1% and 99.8%, respectively (Table 20). The overall sensitivity and specificity for NG were 94.4% and >99.9%, respectively (Table 21). The following table shows PPV and NPV for female urine specimens using hypothetical prevalence rates.

Table 28: Hypothetical PPV and NPV– Female Urine

Prevalence Rate (%)	CT				NG			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	98.1	99.8	85.5	100	94.4	>99.9	97.3	99.9
2	98.1	99.8	92.2	100	94.4	>99.9	98.6	99.9
5	98.1	99.8	96.8	99.9	94.4	>99.9	99.5	99.7
10	98.1	99.8	98.5	99.8	94.4	>99.9	99.7	99.4
15	98.1	99.8	99.0	99.7	94.4	>99.9	99.8	99.0
20	98.1	99.8	99.3	99.5	94.4	>99.9	99.9	98.6
25	98.1	99.8	99.5	99.4	94.4	>99.9	99.9	98.2
30	98.1	99.8	99.6	99.2	94.4	>99.9	99.9	97.7
50	98.1	99.8	99.8	98.1	94.4	>99.9	100	94.7

In male urine specimens, the overall sensitivity and specificity for CT were 98.5% and 99.8%, respectively (Table 20). The overall sensitivity and specificity for NG were 98.3% and 99.9%, respectively (Table 21). The following table shows PPV and NPV for male urine specimens using hypothetical prevalence rates.

Table 29: Hypothetical PPV and NPV– Male Urine

	CT				NG			
Prevalence Rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	98.5	99.8	82.2	100	98.3	99.9	91.7	100
2	98.5	99.8	90.3	100	98.3	99.9	95.7	100
5	98.5	99.8	96.0	99.9	98.3	99.9	98.3	99.9
10	98.5	99.8	98.1	99.8	98.3	99.9	99.2	99.8
15	98.5	99.8	98.8	99.7	98.3	99.9	99.5	99.7
20	98.5	99.8	99.1	99.6	98.3	99.9	99.6	99.6
25	98.5	99.8	99.3	99.5	98.3	99.9	99.7	99.4
30	98.5	99.8	99.5	99.3	98.3	99.9	99.8	99.3
50	98.5	99.8	99.8	98.5	98.3	99.9	99.9	98.3

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert CT/NG Assay is substantially equivalent to the predicate devices.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

DEC 2 7 2012

Cepheid®
c/o Kerry Flom, Ph.D.
Senior Vice President, Clinical Affairs and Regulatory Submissions
904 Caribbean Drive
Sunnyvale, CA 90489

Re: k121710
Xpert® CT/NG
Regulation Number: 21 CFR 866.3390
Regulation Name: Neisseria spp. direct serological test reagents
Regulatory Class: Class II
Product Code: LSL, MKZ, OOI
Dated: December 10, 2012
Received: December 11, 2012

Dear Dr. Flom:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

4.0 Indications for Use Statement

Indications for Use Form

510(k) Number (if known): K121710

Device Name: Xpert® CT/NG

Indications for Use:

The Xpert® CT/NG Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* real-time PCR test for the automated detection and differentiation of genomic DNA from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) to aid in the diagnosis of chlamydial and gonorrheal urogenital disease. The assay may be used to test the following specimens from asymptomatic and symptomatic individuals: female and male urine, endocervical swab, and patient-collected vaginal swab (collected in a clinical setting).

Ancillary Collection Kits Indications for Use:

The Cepheid® Xpert® CT/NG Vaginal/Endocervical Specimen Collection Kit is designed to collect, preserve and transport patient *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in endocervical and vaginal specimens from symptomatic and asymptomatic individuals prior to analysis with the Cepheid Xpert CT/NG Assay.

The Cepheid® Xpert® CT/NG Urine Specimen Collection Kit is designed to preserve and transport *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in first-catch male and female urine specimens from symptomatic and asymptomatic individuals prior to analysis with the Cepheid Xpert CT/NG Assay.

Prescription Use ___X____ (Part 21 CFR 801 Subpart D)	AND/OR	Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K121710